EXHIBIT
H

QUINTILES

Quintiles, Inc.
Post Office Box 9708
Kansas City, MO 64134-0708
(816) 767-6000

June 3, 2002

Central Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
12229 Wilkins Avenue
Rockville, MD 20852

Subject: **Investigational New Drug Application BSF 208075 for Pulmonary Arterial Hypertension** **Serial No. 000 (Initial Submission)**

Dear Sir or Madam:

On behalf of Myogen, Inc., Quintiles, Inc. is submitting with this correspondence an initial Investigational New Drug Application (IND) for a new chemical entity, BSF 208075, an ET_A selective endothelin receptor antagonist, being investigated in patients with pulmonary arterial hypertension. In accordance with 21 CFR Part 312 this thirty volume IND is submitted in triplicate.

To aid in the evaluation of the application, Section 10 of this IND contains additional information regarding communication with the Division of Cardio-Renal Drug Products that took place previously under IND 63,412. This includes a summary of the actions taken by Myogen in response to the Division's recommendations and copies of correspondence and meeting minutes that discussed the investigation of BSF 208075 for the indication of pulmonary arterial hypertension. In addition, Section 11 of this IND contains a copy of the informed consent form for protocol AMB-220, which is submitted in Section 6.

Also, please find enclosed for submission a letter from Myogen, Inc. transferring the responsibility as US Agent and Authorized Representative to Quintiles, Inc.; a letter from Quintiles accepting the transfer of responsibility; and an official Transfer of US Regulatory Obligations form delineating the duties being transferred.

Any questions concerning this Investigational New Drug Application should be directed to:

Marguerite Enlow, Pharm.D., RAC
Associate Regulatory Director,
Regulatory and Technical Services
Quintiles, Inc.
P.O. Box 9708
Kansas City, MO 64134-0708
Telephone: (816) 767-6408
Fax: (816) 767-7373

Sincerely,

Cynthia Kirk, Ph.D., RAC
Executive Director
Regulatory and Technical Services
Quintiles, Inc. Kansas City

Innovative therapies targeting heart muscle disease

Myogen

June 3, 2002

Douglas Throckmorton, M.D.
Director, Division of Cardio-Renal Drug Products
Center for Drug Evaluation and Research (HFD-110)
Food and Drug Administration

Subject: **BSF 208075**
Selective Endothelin Receptor Antagonist
For Pulmonary Arterial Hypertension

General Correspondence:
Transfer of responsibility as US Agent and Authorized Representative

Dear Dr. Throckmorton:

Effective June 3, 2002, Myogen, Inc. is authorizing Quintiles, Inc., Kansas City, MO to act as its U.S. Agent and Authorized Representative for BSF 208075, an ETA Selective Endothelin Receptor Antagonist, being investigated in patients with pulmonary arterial hypertension. The duties to be performed by Quintiles, Inc. are:

- Submission of the IND
- Verbal and written interaction with the FDA
- Conduct of meetings with the FDA
- Submission of the IND annual reports
- Submission of IND amendments
- General IND maintenance

The contact person at Quintiles, Inc., is:

Marguerite Enlow, Pharm.D., RAC
Associate Regulatory Director,
Regulatory and Technical Services
Quintiles, Inc.
P.O. Box 9708
Kansas City, MO 64134-0708
Telephone: (816) 767-6408
Fax: (816) 767-7373

If you have any questions regarding the above information, please do not hesitate to contact me at Myogen, Inc., 7577 West 103rd Ave. #212, Westminster, CO 80021-5426, telephone (303) 464-5221.

Sincerely,

J. William Freytag
President, CEO and Chairman
Myogen, Inc.

7575 W. 103rd Ave suite #102 • Westminster, CO 80021-5426• Phone: 303-410-6666 • Fax: 303-410-6667

QUINTILES

Quintiles, Inc.
Post Office Box 9708
Kansas City, MO 64134-0708
(816) 767-6000

June 3, 2002

Douglas Throckmorton, M.D.
Director, Division of Cardio-Renal Drug Products
Center for Drug Evaluation and Research (HFD-110)
Food and Drug Administration

Subject: **BSF 208075**
Selective Endothelin Receptor Antagonist
For Pulmonary Arterial Hypertension

General Correspondence:
Acceptance of responsibility as US Agent and Authorized Representative

Dear Dr. Throckmorton:

Effective June 3, 2002, Quintiles, Inc., Kansas City, MO assumes the responsibility from Myogen, Inc. as the U.S. Agent and Authorized Representative for BSF 208075, an ET_A Selective Endothelin Receptor Antagonist, being investigated in patients with pulmonary arterial hypertension. The duties to be performed by Quintiles, Inc. are:

- Submission of the IND
- Verbal and written interaction with the FDA
- Conduct of meetings with the FDA
- Submission of the IND annual reports
- Submission of IND amendments
- General IND maintenance

The contact person at Quintiles, Inc., is:

Marguerite Enlow, Pharm.D., RAC
Associate Regulatory Director,
Regulatory and Technical Services
Quintiles, Inc.
P.O. Box 9708
Kansas City, MO 64134-0708
Telephone: (816) 767-6408
Fax: (816) 767-7373

If you have any questions regarding the above information, please do not hesitate to contact me at Quintiles, Inc., P.O. Box 9708, Kansas City, Missouri 64134-0708, telephone (816) 767-6493.

Sincerely,

Cynthia Kirk, Ph.D., RAC
Executive Director
Regulatory and Technical Services
Quintiles, Inc. Kansas City

TRANSFER OF US FDA REGULATORY OBLIGATIONS FOR INVESTIGATIONAL PHARMACEUTICAL AND BIOLOGIC PRODUCTS UNDER AN INVESTIGATIONAL NEW DRUG (IND) APPLICATION (21 CFR 312.52)

Sponsor:	Myogen	Project Code/ Work Order Number:	Not Assigned
Product Name:	BSF 208075	IND Number:	Not Available
Indication:	Pulmonary Arterial Hypertension	Protocol Number:	All protocols

Responsibility	21 CFR Reference	Obligation Assigned to:	
		Sponsor	Quintiles
A. 1. Preparation of all or part of an IND application	312.23	X	X
2. Submission of IND application to FDA		☐	X
B. Maintain an IND with the following amendments, as necessary:			
1. Preparation of Protocol amendments (includes new protocols, changes in protocols, adding new investigators)	312.30	X	☐
2. Preparation of Chemistry, Manufacturing, and Control amendments	312.31	X	☐
3. Preparation of Pharmacology and Toxicology amendments	312.31	X	☐
4. Preparation of Clinical amendments	312.31	X	☐
5. Safety Reports	312.32		
(a) Preparation of initial report		X	☐
(b) Preparation of follow-up reports		X	☐
(c) Notifications to FDA (phone/fax or written)		☐	X
(d) Notifications to investigators		X	☐
6. Preparation of Annual Reports	312.33	X	X
7. Preparation of response to request for information or clinical hold	312.41, 42	X	X
8. Preparation of letter to withdraw an IND	312.38	X	X
9. **Act as IND agent; submit all amendments to FDA**	312.23 -.42	☐	X
C. Selecting investigators and monitors	312.53		
1. Select qualified investigators[1]	312.53 (a)	X	☐
2. Control of drug[1]			
(a) Approve drug shipment after review of required information from investigator (including signed Form FDA 1572, CV)	312.53 (c)	X	☐
(b) Ship drug to approved investigators	312.53 (b)	☐	X
3. Provide qualified monitors[1]	312.53 (d)	X	☐

	4. Informing investigators[1]			
	(a) Review with investigators their regulatory responsibilities	312.60 -.69	X	☐
	(b) Supply investigator's brochure	312.55 (a)	X	☐
	(c) Inform investigators of new safety information about the study drug	312.55 (b)	X	☐
D.	Review of ongoing investigations	312.56		
	1. Monitoring the investigation (includes ensuring that investigator is complying with all commitments in Section 9 of the signed Form FDA-1572)[1]	312.56(a)	X	☐
	2. Discontinue investigator participation if not compliant[1] Note: If the sponsor does not discontinue an investigator who Quintiles believes to be significantly non-compliant, Quintiles will request a complete transfer of regulatory obligation for that site back to the sponsor.	312.56(b)	X	☐
	3. Initial evaluation of all adverse events[1]	312.56 (c)	X	☐
	4. Upon discontinuation of a study[1]:	312.56 (d)		
	(a) Notify FDA		☐	X
	(b) Notify IRBs and investigators		X	☐
	(b) Assure disposition of drug from sites to sponsor		X	☐
E.	Recordkeeping and record retention	312.57		
	1. Maintain sponsor records and reports for 2 years after study end or marketing application approved, for	312.57(a)(b)		
	(a) Records of drug shipment and disposition		X	☐
	(b) All correspondence with sponsor, FDA, IRB, investigators		X	☐
	(c) Records concerning adverse effects		X	☐
	(d) Other records required by FDA		X	☐
	2. Retain reserve samples of test articles and reference standards used in bioequivalence or bioavailability studies	312.57 (c)	X	☐
F.	Disposition of unused supply of investigational drug	312.59		
	1. Assure return of drug from site to sponsor[1]		X	☐
	2. Conduct final disposition or destruction of drug[1]		X	☐
G.	If requested by FDA, submission of sponsor's records and reports to FDA for inspection	312.58 (a)	X	X
H.	Apply for FDA approval to export investigational drug if:	312.110	☐	☐
	(a) Drug is not approved for marketing in any country, AND			
	(b) Drug is not under an active IND, AND			
	(c) Drug is not being exported to one of listed countries[2]			
	X Not applicable			
I.	Represent sponsor in resolution of disputes with FDA	312.48	X	X
J.	Obtain investigator financial disclosure information	[FR 2/2/98]	X	☐

Sponsor's name
Project code

[1] If responsibility for an item is shared between the sponsor and Quintiles, both boxes will be checked. Quintiles' responsibility for the item is limited to the list of sites attached to this document. **This must be confirmed in the contract.**

[2] Listed countries: Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, and current member nations of the European Union and European Economic Area.

According to 21 CFR 312.52(b), "A contract research organization that assumes any obligation of a sponsor shall comply with the specific regulations in this chapter applicable to this obligation and shall be subject to the same regulatory action as a sponsor for failure to comply with any obligation assumed under these regulations." The assignment of responsibility does not preclude either the sponsor or the CRO from participating in the requirements of the CFR.

The sponsor hereby transfers to Quintiles, Inc. the responsibilities indicated above under the column titled "Obligation Assigned to QUINTILES," effective Jan 15 2002 (date).

Sponsor: MYOGEN	QUINTILES
[signature]	Marguerite Enlow, M.D.
Signature	Regulatory & Technical Services Signature
J. William Freytag	Marguerite Enlow
Printed Name	Printed Name
President, CEO and Chairman	Associate Director
Title	Title
1-15-02	1/15/02
Date	Date